said kit further comprising labeling indicating that the kit can be used to reduce the incidence or severity of a chronic immune-mediated disorder in a mammal, and instructions for the prophylactic or therapeutic use of said immunogens to reduce the incidence or severity of a chronic immune-mediated disorder in a mammal to which one or more doses of said immunogens are administered according to an immunization schedule set forth in said instructions,

said immunogens, when so administered, acting to substantially reduce the incidence or severity of said chronic immune-mediated disorder,

wherein said schedule, according to said instructions, calls for the first dose of an immunogen to be given before 42 days ~~after birth.~~

In claims 39-40, please replace "kit" with --method-- and "38" with --41--.

Please rewrite claim 3 as follows:

3 (twice amended). A method of immunizing a mammal less than 96 months of age against at least one infectious disease, while decreasing the incidence of an autoimmune disease [diabetes mellitis or systemic lupus erythrematosis], comprising

administering to said mammal one or more pharmaceutically acceptable pharmaceutical preparations, comprising one or more immunogens, according to an immunization schedule according to which, at specific times after birth, the mammal receives one or more pharmaceutically acceptable doses of one or more immunogens;

said mammal thereby receiving, for each said infectious disease, a suitable immunogen in such amounts, given at such ages, as to be effective to substantially prevent or substantially reduce the severity of such infectious disease;

said administering further resulting in an immune response in said mammal sufficient to substantially reduce the incidence of [diabetes mellitis] an autoimmune disease in such mammals;

said mammals are selected from the group consisting of humans, and nonhuman mammals which are animal models of a human autoimmune disease,

where, when all of the immunogens administered are selected from the group consisting of BCG, diphtheria, tetanus, whole cell pertussis, polio, hepatitis B, hemophilus influenza, measles, mumps and rubella immunogens, at least one of the following conditions applies: (a) immunogens are administered on at least three different dates prior to 42 days after birth, or (b) immunogens are administered on at least three different dates, and the maximum interval between administrations is about two weeks, or less. [for at least one such immunogen, either

(a) a plurality of doses of the immunogen are administered, and such doses are administered less than 28 days apart, or

(b) the immunogen is a live polio virus and at least five doses are given during the first 112 days after birth, or

(c) the immunogen is not a live polio virus, and at least four doses are given during the first 112 days after birth.]

In claims 2, and 11-14, replace "diabetes" with -autoimmune disease--.

Please rewrite claims 21, 23, 24, 25, 26, 28, 30, 33 and 37, as follows:

19. (twice amended). In a method for immunization against at least three infectious diseases, comprising administering at least one pharmaceutically acceptable dose of diphtheria/ tetanus/pertussis vaccine to a mammal of at least 42 days of age, the improvement comprising:

further administering to said mammal at least one pharmaceutically acceptable dose of diphtheria/pertussis/ tetanus vaccine, wherein said further administration is according to at least one step selected from the group consisting of

(1) administrating at least two doses of said diphtheria/tetanus/pertussis vaccine at less than 42 days of age

of said mammal;

(2) administering said at least one of said dose of said diphtheria/tetanus/pertussis vaccine at less than 42 days of age of said mammal and also administering at least a second dose of said diphtheria/tetanus/pertussis vaccine, said second dose or any subsequent dose administered less than 28 days after the preceding dose when said mammal is less than 175 days of age; and

(3) administering said at least one dose of said diphtheria/tetanus/pertussis vaccine at less than 42 days of age of said mammal and also administering as a total of at least four doses of said diphtheria/tetanus/pertussis vaccine prior to the age of 112 days of said mammal,

wherein the further administration reduces the incidence of diabetes mellitis in a population and/or subpopulation of said mammals,

where said mammal is a human, or an animal model of a human diabetes, and is not a streptozocin-treated mouse, and said mammal receives at least one of the following immunogens prior to age of 24 months: hepatitis B, hemophilus influenza B, mumps, rubella, chicken pox, acellular pertussis, and pneumococcus immunogens.

21. ~~(amended)~~ (twice amended). In a method for immunization against at least two infectious diseases, comprising administering at least one pharmaceutically acceptable dose of diphtheria/tetanus/pertussis vaccine and at least one pharmaceutically acceptable dose of hemophilus influenza vaccine to a mammal of at least 42 days of age, the improvement comprising:

~~and~~ further administering to said mammal at least one pharmaceutically acceptable dose of at least one of a diphtheria/pertussis/tetanus vaccine and a hemophilus influenza vaccine wherein said further administration ~~and~~ is according to

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at least one method from the group consisting of

(1) administrating at least one dose of both said diphtheria/pertussis/tetanus vaccine and said hemophilus influenza vaccine at less than 42 days of age of said mammal and at least a second dose of at least one said vaccine prior to 42 days of age of said mammal;

(2) administering at least one of said dose of both said diphtheria/tetanus/pertussis vaccine and said hemophilus influenza vaccine at less than 42 days of age of said mammal and also administering at least a second dose of both of said vaccines, wherein said second dose and or any subsequent dose is administered at less than 42 days after the preceding dose when said mammal is less than 175 days of age; and

(3) administering at least one of said dose of both said diphtheria/tetanus/pertussis vaccine and said hemophilus influenza vaccine at less than 42 days of age of said mammal and administrating at least four doses, prior to the age of 112 days, of said mammal for said diphtheria/pertussis/ tetanus vaccine or said hemophilus influenza vaccine, the incidence of diabetes mellitis in a population and/or subpopulation of said mammals, where said mammal is a human, or an animal model of a human diabetes, and is not a streptozocin-treated mouse, and said mammal receives at least one of the following immunogens prior to age of 24 months: hepatitis B, hemophilus influenza B, mumps, rubella, chicken pox, acellular pertussis, and pneumococcus immunogens.

E4 cont'd

22. ~~(amended)~~ (twice amended). In a method for immunization against at least two infectious diseases, comprising administering at least one pharmaceutically acceptable first dose of at least one pharmaceutically acceptable immunogen selected from the group consisting of a diphtheria/tetanus/pertussis immunogen, a polio immunogen, a hepatitis B immunogen, a hemophilus influenza immunogen, a non-pediatric immunogen, and a measles/mumps/rubella

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immunogen, to a mammal after 112 days of age but prior to 724 days of age, the improvement comprising:

~~(a)~~ further administering to said mammal, prior to the age of 112 days, at least one pharmaceutically acceptable second dose containing a greater amount of said immunogen than the amount of immunogen administered as said first dose after 112 days of age but prior to 724 days of age of said mammal, wherein the further administration reduces the incidence of diabetes mellitis in a population and/or subpopulation of said mammals,

where said mammal is a human, or an animal model of a human diabetes, and is not a strepzocin-treated mouse, and said mammal receives at least one of the following immunogens prior to age of 24 months: hepatitis B, hemophilus influenza B, mumps, rubella, chicken pox, acellular pertussis, and pneumococcus immunogens.

23 ~~22~~ (twice amended). In a method for immunization against at least two infectious diseases, comprising administering at least one pharmaceutically acceptable dose of a non-whole cell pertussis vaccine to a mammal at least 42 days of age but prior to 724 days of age, the improvement comprising

~~(a)~~ further administering to said mammal at least one pharmaceutically acceptable dose of at least one pharmaceutically acceptable immunogen selected from the group consisting of an diphtheria/tetanus immunogen, a non-whole cell pertussis immunogen, a whole cell pertussis immunogen, a polio immunogen, a hemophilus influenza immunogen, a measles/mumps/rubella immunogen and a non-pediatric immunogen, wherein said further administration ~~is~~ is according to at least one selected from the group consisting of

(1) administrating said at least one dose of said immunogen at less than 42 days of age of said mammal;

(2) administering said at least one dose of said immunogen, said dose comprising at least a second dose, said

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second dose or any subsequent said dose administered less than 28 days after the preceding dose when said mammal is less than 175 days of age; and

(3) administrating at least four doses prior to the age of 112 days of said mammal, wherein the further administration reduces the incidence of diabetes mellitis in a population and/or subpopulation of said mammals,

where said mammal is a human, or an animal model of a human diabetes, and is not a streptozocin-treated mouse, and said mammal receives at least one of the following immunogens prior to age of 24 months: hepatitis B, hemophilus influenza B, mumps, rubella, chicken pox, acellular pertussis, and pneumococcus immunogens.

24. ~~(amended)~~ (twice amended). In a method for immunization against at least two infectious diseases, comprising administering at least one pediatric vaccine to a mammal of at least 42 days of age, the improvement comprising:

~~(a)~~ further administering to said mammal at least one pharmaceutically acceptable dose of at least one pharmaceutically acceptable vaccine selected from (i) a combined vaccine containing at least diphtheria, tetanus, pertussis, and hemophilus influenza immunogens, and (ii) a combined vaccine containing at least diphtheria, tetanus, pertussis, and hepatitis B immunogens,

wherein said further administration ~~(a)~~ is according to at least one step selected from the group consisting of

(1) administrating at least of one of said dose of said combined vaccine at less than 42 days of age of said mammal;

(2) administering at least one of said dose of said combined vaccine, said dose comprising at least a second dose, said second dose or any subsequent dose administered less than 28 days after the preceding dose when said mammal is less than 175 days of age; and

(3) administrating at least four doses prior to the age of 112 days of said mammal,

wherein the further administration reduces the incidence of diabetes mellitis in a population and/ or subpopulation of said mammals,

where said mammal is a human, or an animal model of a human diabetes, and is not a streptozocin-treated mouse, and said mammal receives at least one of the following immunogens prior to age of 24 months: hepatitis B, hemophilus influenza B, mumps, rubella, chicken pox, acellular pertussis, and pneumococcus immunogens.

25 ~~23~~ (twice amended). In a method for pediatric immunization against at least two infectious diseases, comprising administering at least one pharmaceutically acceptable dose of at least one pediatric vaccine to a mammal of at least 42 days of age,

the improvement comprising:

~~(a)~~ further administering to said mammal at least one pharmaceutically acceptable supraimmunogenic dose of at least one pharmaceutically acceptable vaccine prior to the age of 112 days of said mammal,

wherein the further administration reduces the incidence of diabetes mellitis in a population and/or subpopulation of said mammals,

where said mammal is a human, or an animal model of a human diabetes, and is not a streptozocin-treated mouse, and said mammal receives at least one of the following immunogens prior to age of 24 months: hepatitis B, hemophilus influenza B, mumps, rubella, chicken pox, acellular pertussis, and pneumococcus immunogens.

27 ~~25~~ (twice amended). In a method for immunization against at least two infectious diseases, comprising administering at least one pharmaceutically acceptable dose of at least one

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pediatric vaccine to a mammal of at least 42 days of age, the improvement comprising:

(a) further administering to said mammal at least one pharmaceutically acceptable dose of at least one pharmaceutically acceptable immunogen to said mammal prior to the age of 8 days; and

(b) further administering at least one pharmaceutically acceptable dose of at least one pharmaceutically acceptable immunogen to said mammal at least 11 days of age but less than 26 days of age,

wherein the further administrations reduce the incidence of diabetes mellitis in a population and/or subpopulation of said mammals,

where said mammal is a human, or an animal model of a human diabetes, and is not a streptozocin-treated mouse, and said mammal receives at least one of the following immunogens prior to age of 24 months: hepatitis B, hemophilus influenza B, mumps, rubella, chicken pox, acellular pertussis, and pneumococcus immunogens.

30. (twice amended). In a method for immunization against at least two infectious diseases, comprising administering at least one pharmaceutically acceptable dose of at least one pharmaceutically acceptable immunogen to a mammal, the improvement comprising:

further administering at least a second separate pharmaceutically acceptable dose of at least one pharmaceutically acceptable immunogen, said second dose and or any subsequent dose is administered less than 28 days after the preceding dose, wherein said second or any subsequent dose contains the same or different immunogens or the same or different amounts of said immunogens as any other dose; (ii) each said separate dose is administered during a 0-78 hour period, and (iii) the further administration reduces the incidence of diabetes mellitis in a

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population and or subpopulation of said mammals,

where said mammal is a human, or an animal model of a human diabetes, and is not a streptozocin-treated mouse, and said mammal receives at least one of the following immunogens prior to age of 24 months: hepatitis B, hemophilus influenza B, mumps, rubella, chicken pox, acellular pertussis, and pneumococcus immunogens.

32. (twice amended). A method of immunizing a mammal less than 96 months of age against at least two infectious ~~disease~~ diseases and at least one chronic immune-mediated disorder, comprising

administering to said mammal one or more pharmaceutically acceptable pharmaceutical preparations, comprising one or more immunogens, according to an immunization schedule according to which, at specific times after birth, the mammal receives one or more pharmaceutically acceptable doses of one or more immunogens;

said mammal thereby receiving, for each said infectious disease, a suitable immunogen in such amounts, given at such ages, as to be effective to substantially prevent or substantially reduce the severity of such infectious disease;

said administering further resulting in an immune response in said mammal sufficient to substantially reduce the incidence of diabetes mellitis in such mammal;

the first dose of said immunization schedule including an immune modulator beginning 42 days before birth,

where said mammal is not immunized with an immunogen in such amounts and at such times as would substantially induce diabetes mellitis,

where said mammal is a human, or an animal model of a human diabetes, and is not a streptozocin-treated mouse, and said mammal receives at least one of the following immunogens prior to age of 24 months: hepatitis B, hemophilus influenza B, mumps, rubella, chicken pox, acellular pertussis, and pneumococcus immunogens.

Please add the following claims:

42. The method of claim 3 in which the autoimmune disease is diabetes or systemic lupus erythrematosis.

43. The method of claim 41 in which the mammal is a human.

44. The method of claim 41 in which the mammal is an animal model of diabetes or systemic lupus erythrematosis.

45. A method according to claim 41, wherein at least one of said immunogens is an immunogen selected from the group consisting of an anthrax immunogen, a small pox immunogen, a pneumococcal immunogen, a cholera immunogen, a varicella immunogen, a typhoid immunogen, a yellow fever immunogen, a neisseria immunogen, a plague immunogen, an influenza immunogen, a herpes immunogen, a meningitis immunogen, an adenovirus immunogen, a cytomegalovirus immunogen, a hepatitis C immunogen, rabies and a molecule that cross reacts to any of said immunogens.

46. The method of claim 41 wherein the first dose is ~~administered before 28 days after birth~~.

47. The method of claim 41 wherein at least four doses are administered before 42 days after birth.

48. The method of claim 41, wherein no tolerogen is administered prior to 42 days after birth.

49. The method of claim 41 where ~~said labeling indicates~~ that starting the ~~first~~ dose of ~~immunization~~ after 56 days after birth ~~may~~ not reduce said chronic immune mediated disorder or may ~~increase the risk of said chronic immune mediated disorder.~~

50. A method of immunizing a mammal less than 24 months of age against at least 2 infectious disease and diabetes mellitus, comprising administering to said mammal one or more pharmaceutically acceptable pharmaceutical preparations, comprising one or more immunogens, according to an immunization schedule according to which, at specific times after birth, the mammal receives one or more pharmaceutically acceptable doses of

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two or more immunogens;
said mammal thereby receiving, for each said infectious disease, a suitable immunogen in such amounts, given at such ages, as to be effective to substantially prevent or substantially reduce the severity of such infectious disease;
said administering further resulting in an immune response in said mammal sufficient to substantially reduce the incidence of diabetes mellitus in such mammal;
where said mammal is a human, or an animal model of a human diabetes, and is not a streptozocin-treated mouse;
the first dose of at least 2 immunogens are given before 42 days after birth;
and where said mammal receives at least one of the following immunogens: hepatitis B, haemophilus influenza B, mumps, rubella, varicella, acellular pertussis, and pneumococcus immunogen.

34 ~~51~~. The method of claim ~~50~~ 33 wherein said mammal is a human.

35 ~~52~~. The method of claim ~~50~~ 33 wherein said mammal is not immunized with an immunogen in such amounts and at such times as would increase the incidence of diabetes mellitus.

36 ~~53~~. The method of claim ~~50~~ 33 wherein said 2 immunogens are ones other than a BCG or Hepatitis B immunogen.

37 ~~54~~. The method of claim ~~50~~ 33 wherein more than 2 doses of at least one said immunogen is given prior to 42 days after birth.

38 ~~55~~. The method of claim ~~50~~ 33 wherein the longest interval between doses is less than 28 days.

39 ~~56~~. The method of claim 33 ~~57~~ wherein the first dose is given prior to 15 days after birth.

40 ~~57~~. In a method for immunization against at least two infectious diseases, comprising administering at least one pharmaceutically acceptable dose of a conjugated pneumococcal or varicella vaccine to a mammal at least 42 days of age but prior to 724 days of age, the improvement comprising:

~~(a)~~ further administering to said mammal at least one

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pharmaceutically acceptable dose of at least one pharmaceutically acceptable immunogen selected from the group consisting of a diphtheria tetanus immunogen, a non-whole cell pertussis immunogen, a whole cell pertussis immunogen, a polio immunogen, a hemophilus influenza immunogen, a measles mumps rubella, varicella, pneumococcal and a non-pediatric immunogen, wherein said further administration is according to at least one selected from the group consisting of

(1) administrating said at least one dose of said immunogen at less than 42 days of age of said mammal;

(2) administering said at least one dose of said immunogen, said dose comprising at least a second dose, said second dose or any subsequent said dose administered less than 28 days after the preceding dose when said mammal is less than 175 days of age; and

(3) administrating at least four doses prior to the age of 112 days of said mammal, wherein the further administration reduces the incidence of diabetes mellitus ~~said disorder,~~ in a population and/or subpopulation of said mammals.

58. A method of decreasing the incidence of an autoimmune disease which comprises:

administering to said mammal one or more pharmaceutically acceptable pharmaceutical preparations, comprising one or more immunogens, according to an immunization schedule according to which, at specific times after birth, the mammal receives one or more pharmaceutically acceptable doses of one or more immunogens;

said administering resulting in an immune response in said mammal sufficient to substantially reduce the incidence of an autoimmune disease in such mammals;

said mammals are selected from the group consisting of humans, and nonhuman mammals which are animal models of a human autoimmune disease,

where, when all of the immunogens administered are selected from

the group consisting of BCG, diphtheria, tetanus, whole cell pertussis, polio, hepatitis B, hemophilus influenza, measles, mumps and rubella immunogens, at least one of the following conditions applies: (a) immunogens are administered on at least three different dates prior to 42 days after birth, or (b) immunogens are administered on at least three different dates, and the maximum interval between administrations is about two weeks, or less.

42. The method according to claim 41, wherein at least one of said immunogens is an immunogen selected from the group consisting of an anthrax immunogen, a small pox immunogen, a pneumococcal immunogen, a cholera immunogen, a varicella immunogen, a typhoid immunogen, a yellow fever immunogen, a neisseria immunogen, a plague immunogen, an influenza immunogen, a herpes immunogen, a meningitis immunogen, an adenovirus immunogen, a malaria immunogen, an HIV immunogen, a cytomegalovirus immunogen, a hepatitis C immunogen, a rabies immunogen and a molecule that cross reacts to any of said immunogens.

REMARKS

Overview of Claim Amendments

Claim 3 has been amended in several respects:

(1) it is not limited to diabetes or SLE. Instead, it is directed to use to reduce the incidence of any autoimmune disease. Note that original claim 1 was originally even broader (it was directed to any chronic immune-mediated disorder), and that original claim 15 recited "autoimmune disease".

(2) it requires that the mammals receiving the therapy be either humans, or nonhuman mammals which are animal models of a human autoimmune disease (by way of example, NOD mice are animal models of human insulin-dependent diabetes mellitis).

(3) it modifies the proviso applicable when all of the